Bioconjugate Chemistry

Review

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Self-Assembly of Peptide Bioconjugates: Selected Recent Research Highlights

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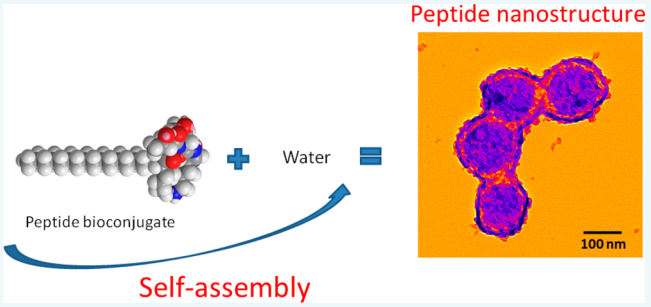
ABSTRACT: This Topical Review briefly discusses selected highlights of recent research on self-assembling peptide amphiphiles (PAs) and polymer−peptide conjugates. Subjects covered include new polymer chemistries used to prepare polymer−peptide conjugates, PA self-assembly landscapes and kinetics, developments in the application of bioactive PAs and the relationship between self-assembly and bioactivity, novel PA/biopolymer composites, functional π-stacking peptide conjugates, use of enzymes to tune self-assembly, and developments in high throughput methods and the design and application of sequenced peptides.



1. INTRODUCTION

Peptide conjugates combine the biofunctionality and diverse structural epitopes of peptides with nonpeptidic moieties such as polymer or lipid chains, in order to adjust self-assembly behavior. This enables access to nanostructures outside the range of canonical peptide secondary and tertiary structures and leads to the creation, for example, of fibrillar, micellar, and vesicular structures with high density peptide coatings. A large number of therapeutically relevant applications are being uncovered for such systems and this is driving ongoing intense research activity in the field.

This Topical Review highlights selected recent developments in the field of self-assembling peptide conjugates including polymer−peptide conjugates, amphiphilic peptides, and peptide amphiphiles (PAs). By its nature, it is not intended to be comprehensive, and inevitably there is not sufficient space to discuss all of the exciting progress in the field. This Topical Review complements a recent short review on bioactive lipopeptides, focused on biologically derived, mainly cyclic lipopeptides.[1] In this review, we discuss developments in polymer−peptide conjugates, in particular focused on the synthesis of conjugates with alternatives to PEG [PEG: polyethylene glycol]. Then we discuss the kinetics of self-assembly and its relationship to the thermodynamic landscape. This is followed by a brief summary of recent work in the highly researched field of bioactive peptide amphiphiles, which have important potential biomedical applications, and on the relationship between self-assembly and bioactivity and then of PA/biopolymer composites. This is followed by brief accounts of recent work on functional π-stacking peptide conjugates, the use of enzymes to tune peptide self-assembly, high throughput methods, and sequenced peptides.

The subjects of self-assembly of surfactant-like peptides and peptide amphiphiles have recently been reviewed.[2−6] In addition, the formation of peptide nanotubes has been reviewed.[7] On the specific subject of PEG−peptide conjugates, a number of useful reviews are available,[8] as are a range of comprehensive reviews of polymer−peptide conjugates more broadly.[9−13]

2. POLYMER−PEPTIDE CONJUGATES: BEYOND PEG

Although PEG has been widely used as a conjugating polymer due to advantages in stability, low cost, and inertness, it can lead to immunogenicity; it is not very biodegradable and may undergo peroxidation with damaging effects for cells and tissues.[14,15] PEGylation of proteins and peptides is performed in order to increase circulation time in a "stealth"-like fashion. Therefore, a variety of alternatives, prepared via living polymerization methods, for example, have been considered, such as poly(2-oxazoline)s, poly(*N*-hydroxypropyl methacrylamide), or oligo-ethylene glycol methacrylates (OEGMAs) (Figure 1).[14,15]

An attractive and widely used set of methods to conjugate polymers and peptides is so-called "click" reactions, including copper-catalyzed alkyne−azide cycloaddition. This subject is reviewed in detail elsewhere,[16] and these and other methods to synthesize PEG-peptides have been summarized.[8] In one interesting example, copper-catalyzed alkyne−azide cycloaddition has been combined in a single pot reaction with enzymatic transamidation, which catalyzes acyl transfer between glutamine and lysine residues, in order to prepare peptide conjugates.[17] In another recent study, direct thiol−ene coupling was used to lipidate TLR (Toll-like receptor) agonist peptide CSK_4, to produce a self-adjuvating vaccine candidate.[18]

3. PA SELF-ASSEMBLY LANDSCAPES AND KINETICS

The thermodynamics and kinetics of self-assembly (and their inter-relationships) of peptide-based systems such as PAs has

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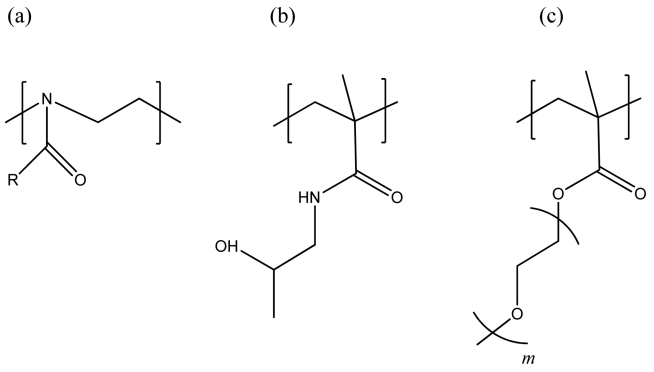

Figure 1. Examples of alternatives to PEG used in polymer–peptide conjugates: (a) polyoxazolines, (b) poly(*N*-hydroxypropyl methacrylamide), (c) oligoethylene glycol methacrylates (OEGMAs).

been relatively unexplored until very recently. However, several interesting reports suggest that this will be a rich field for further investigation. It has been reported that self-assembled β-sheet fibrils of a bioactive PA incorporating a sequence from the extracellular matrix (ECM) proteoglycan lumican[19] can apparently be diluted below the equilibrium critical aggregation.[20] Stability of the "crystallized" PA fibrils and β-sheet secondary structure for up to 1 week was observed, although longer term kinetic and annealing studies are still ongoing. The influence on bioactivity was also studied and a significant increase in collagen production by human corneal fibroblasts was observed for the diluted-aggregated system.[20] Stupp's group have also observed kinetically trapped monodisperse long fibers with β-sheet structure and noted that this behavior was dependent on ionic strength of the solution of the charged PA molecules studied (Figure 2).[21] The thermodynamically stable state (accessed via annealing) at low ionic strength is short monodisperse fibrils with a random coil secondary structure. A kinetically trapped state of long β-sheet fibers can be accessed via dilution from high ionic strength to below a critical ionic strength. Re-annealing drives a transition back to the thermodynamically stable state. At high ionic strength, an energy barrier (obtained from an Arrhenius plot from temperature-dependent rate kinetic measurements) separates the thermodynamic product (monodisperse short fibers without β-sheet secondary structure) from a kinetically trapped state of long β-sheet fibers. This state is observed after annealing and dilution (in that order), and the thermodynamic product can be accessed by subsequent addition of salt to give high ionic strength conditions.

4. DEVELOPMENTS IN THE USE OF BIOACTIVE PEPTIDE AMPHIPHILES

There continue to be remarkable developments in the application of peptide amphiphiles to various biorelated applications, including cell growth and differentiation. In one example, Guler's group produced nanofibers containing mixtures of PAs with GAG-mimetic functionality, a RGD cell adhesion domain, or electrostatic diluent functionality.[22] GAG denotes glycosaminoglycan, a class of biomolecules with sulfonate, hydroxyl, and carboxylate groups which are important components of the extracellular matrix. Osteogenic or chondrogenic differentiation of mesenchymal stem cells was noted dependent on the concentration of media within the bioactive PA nanofiber gels.[22]

Photodynamic control of bioactivity of PA nanofibers has recently been demonstrated.[23] A PA was developed that contains

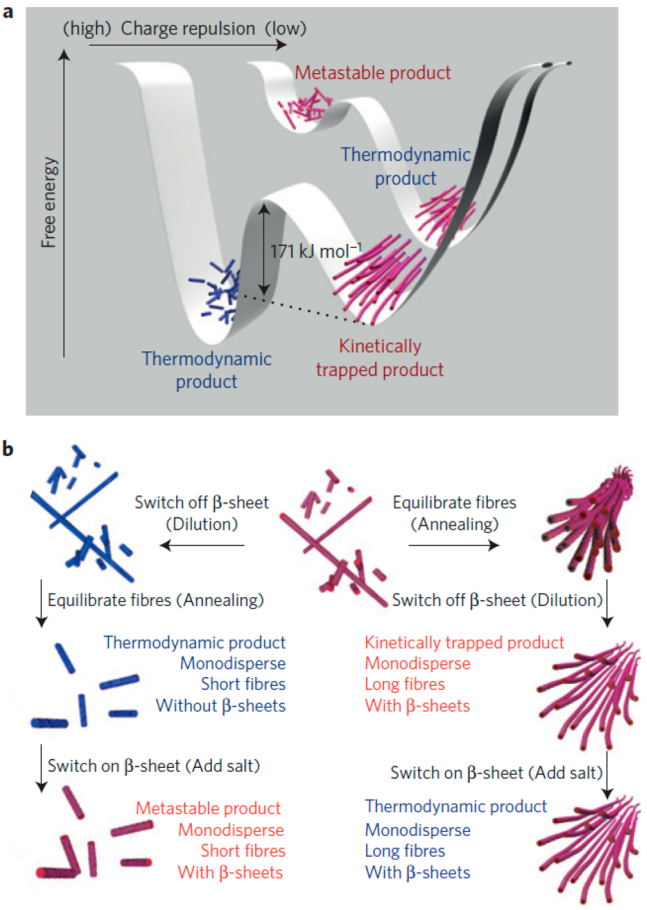

Figure 2. Energy landscapes for self-assembling PAs.[21] (a) Two ionic strengths which modulate PA molecular electrostatic repulsion. (b) Influence of dilution, annealing, and changes in ionic strength on the mode of PA self-assembly. Reprinted by permission from Macmillan Publishers Ltd.: Nature (ref 21), copyright 2016.

a photolabile linker between the RGDS cell adhesion sequence and the rest of the PA molecule (lipopeptide with a peptide sequence to drive β-sheet formation). Fibroblast spreading can be arrested by exposure to light as a result of PA cleavage.[23] In another development, alginate-PA core–shell microparticles have been prepared based on a cross-linked core of doxorubicin-conjugated alginate coated with nanofibers from a PA bearing tumor-targeting folate units.[24] Lack of space here prevents us reviewing the other extensive seminal contributions of the Stupp group to the study of PAs for biomedical applications. In any case, this work has been reviewed by members of this group[6,25,26] and is extensively featured in many other reviews on PAs.

In several types of tissue, the components of the extracellular matrix such as collagen are aligned. It has been shown that aligned PTFE [poly(tetrafluoroethylene)] substrates (having a microgroove structure from controlled rubbing) enhance the proliferation of aligned cells (Figure 3) and increase the complexity of the produced tissue.[27] An optimal composition of mixtures of bioactive PA with "diluent" PA was identified (13%:87% molar ratio), a composition similar to that identified in prior work,[6,28] which is possibly associated with optimal epitope density.[27] In a development of this work, self-releasing aligned tissue films were created based on protease degradation of PAs incorporating MMP (matrix metalloprotease) substrates.[29,30] Tissue equivalents prepared on the aligned substrate had highly ordered, compact collagen deposition, with a 2-fold

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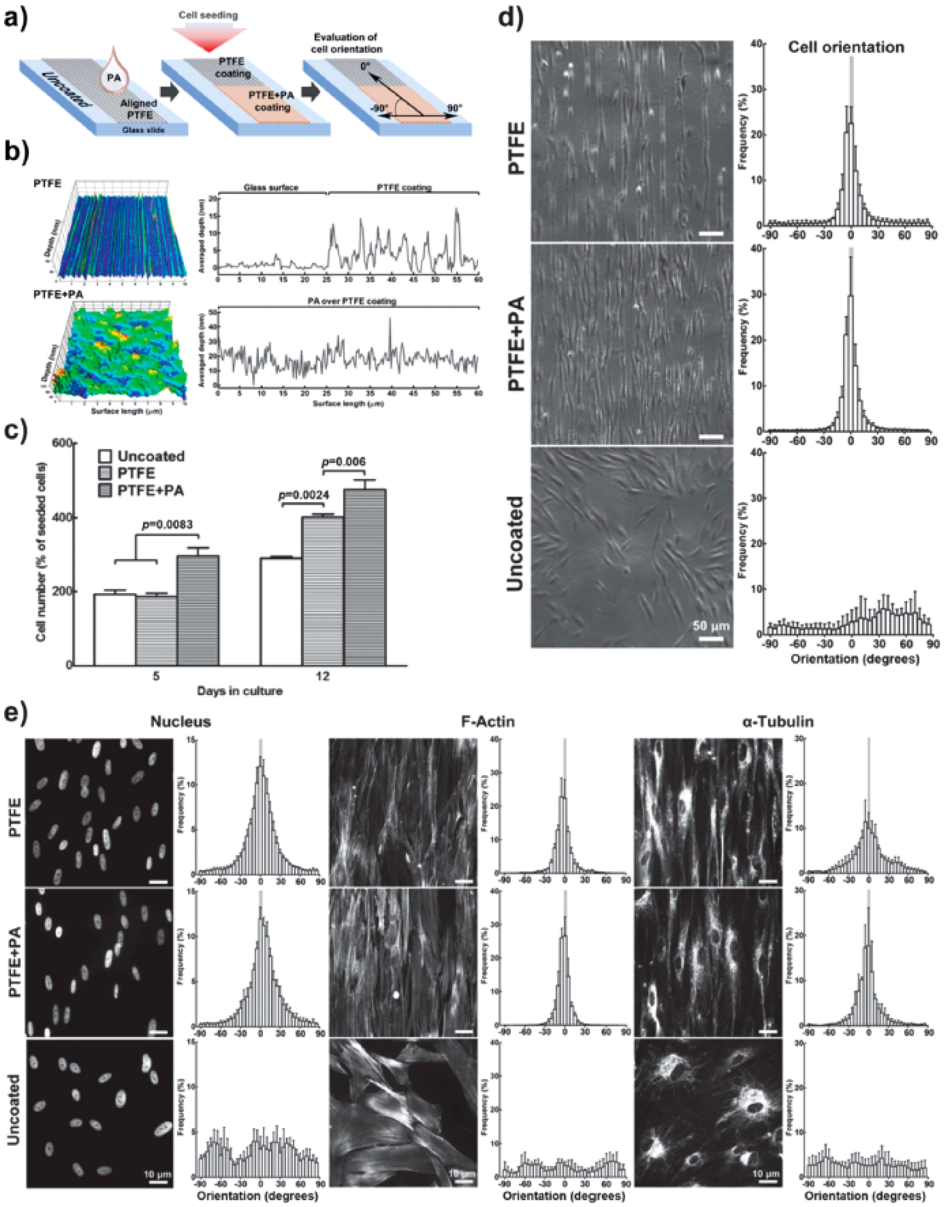

Figure 3. Enhanced cell adhesion on a mixed PA (C_{16}-MMP/C_{16}-ETTES, 13%:87% molar ratio) coating on alignment-inducing PTFE slides.[27] (a) Schematic of PTFE and PTFE+PA coatings, uncoated glass was used as a control. (b) AFM mapping of PTFE and PTFE+PA coatings, with representative cross-section scans. (c) Proliferation of hCSFs cultured at day 5 and day 12 on different coatings. (d) Cell and corresponding (e) nucleus and cytoskeleton orientation of hCSFs cultured for 12 days on PTFE, PTFE + PA, and uncoated glass surfaces using phase-contrast and fluorescence microscopy, respectively. Mean ± S.D., $n = 3$ for all experiments. Scale bars: (d) 50 μm, (e) 10 μm. Reproduced in part from ref 27 with permission of the Royal Society of Chemistry.

higher elastic modulus compared to the less compact tissues produced on the nonaligned template, the PA-coated glass.[29]

Another important application of peptide amphiphiles involves their conjugation to bioactives such as drug molecules. Cui et al. have investigated the formation of fibrils or nanotubes by a short β-sheet peptide derived from the Tau protein linked via a short octyl spacer to the anticancer drug camptothecin.[31] These nanostructures were shown to have antitumor activity against a number of cancer cell lines. Following a similar concept, camptothecin has been conjugated to a short yeast prion peptide (Sup35) along with charged C terminal dipeptide units (two lysine or two glutamic acid residues).[32] The formation of multiwalled nanotubes was observed in catanionic mixtures of these peptide amphiphiles. This group has also investigated the use of a PA containing a TAT [trans-activating transcriptional activator] cell-penetrating peptide sequence (conjugated to four octyl lipid chains) to encapsulate the hydrophobic anticancer drug paclitaxel.[33] A high loading efficiency was noted and increased paclitaxel content led to increased nanofiber flexibility. They also showed that hydrophobic modification (addition of a palmitic acid chain) increased the uptake of a TAT peptide into cancer cells and enhanced anticancer activity of a palmitoylated TAT-doxorobicin conjugate compared to the conjugate without the lipid chain.[34]

For practical applications, the control and stability of self-assembled nanostructures under in vivo conditions is desirable. In one example, it has recently been demonstrated that a lipopeptide bearing anionic (glutamic acid-rich) sequences can self-assemble into nanofibers or micelles in blood serum.[35] The PA undergoes a transition from spherical micelles to nanofibers

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in the pH range 7.0−7.4 in pure blood serum as shown by fluorescence anisotropy measurements on fluorophore-labeled PA molecules.

Another interesting application for peptide nanostructures is in biomedical imaging. Recent highlights (pun intended) in the literature include studies by the Cui and Stupp groups. A peptide-based molecular beacon system has been developed that is able to detect the enzyme cathepsin B due to cleavage of a short substrate sequence and concomitant release of a pendant fluorophore (otherwise quenched due to the presence of a quencher also incorporated in the molecule).[36] The peptide also incorporates a TAT sequence to facilitate uptake into cells. The peptide conjugate self-assembles into micelles, but upon dilution or pH triggering, the monomeric state is accessed and in this form enzyme detection is possible due to exposure of the enzyme degradable linker and fluorophore. A similar peptide conjugate but containing a β-sheet forming heptapeptide sequence (from an amyloid peptide) is able to form spherical micelles or nanofibers (depending on temperature).[37] The spherical form is more readily taken up into cancer cells via endocytosis, permitting in cellulo imaging. The Cui group has also developed dual-mode nanoprobes containing both a fluorophore for optical imaging and a metal ion [Gd(III)] chelator for MRI or radionuclear imaging.[38] The nanoprobes are based on a PA to which both probe groups are attached to lysine residues close to the one or two alkyl chains in the molecules. The molecules self-assemble into nanospheres. This incorporation of Gd-chelators into PAs builds on earlier work on the development of PAs bearing Gd(III) complexes for in situ MRI imaging of the uptake (using a mouse leg model) and for subsequent tracking of the biomaterial after implantation.[39] In this work, the Gd complex was attached, either singly or multiply, at the C-terminus to PAs that self-assemble into nanofibers.

5. RELATIONSHIP BETWEEN SELF-ASSEMBLY AND BIOACTIVITY

The influence of self-assembly on bioactivity has been relatively unexplored to date, at least in terms of studies where bioactivity has been compared for PA in self-assembled and monomeric states. However, a number of recent studies have examined the influence of the shape of self-assembled nanostructures on bioactivity.

The shape of self-assembled peptide nanostructures is known to have an effect on various properties, and recent work has investigated the influence of shape on bioactivity. An earlier review touches on this topic.[40] It is well-known that the shape of micelles (spherical vs rod-like) can influence in vivo delivery properties of therapeutic molecules such as block copolymer self-assemblies trapping drugs,[41] and recent work has extended this concept to PA systems. In one recent study,[42] three PAs were prepared with collagen-binding sequences. In one, a β-sheet driving sequence (alternating A_2V_2 sequence) was included which led to self-assembly into nanofibers in contrast to the spherical micelle assembly of the other two without the A_2V_2 sequence. Nanofibers were shown to bind to a biological target (rat carotid artery injury model) in contrast to the nanospheres. In another very interesting recent study,[43] nanofibers formed by a PA (with a β-sheet forming sequence) were compared to nanospheres formed by related PAs (with proline sequence disfavoring β-sheet formation) in terms of delivery of oligonucleotides (incorporated into the PA nanostructures) into cells. Distinct delivery mechanisms were observed depending on shape and size (which in fact are hard to decouple). Nanofibers were found to deliver more oligonucleotides into cells when examined over an extended period, due to slow diffusion of nanospheres out of cells despite their rapid initial uptake. This group also compared some of the same PA nanostructures in terms of delivery of a DNA sequence within the class of pathogen-associated molecular patterns (PAMPs) characteristic of bacteria and viruses.[44] The authors showed that nanofibers exhibited enhanced uptake compared to nanospheres or the DNA in the absence of any PA assemblies. This work suggests that such structures may be useful in modulating the immune response. A study on self-assembling star polymers with a glycopeptide headgroup showed self-assembly into nanorods, polymersomes, or micelles, depending on the polymer composition.[45] Rods and polymersomes were taken up by breast cancer cells, although in contrast to the studies mentioned above, no significant effect of the shape of the nanostructure on this uptake was noted.

Alternatively, considering whether the monomer or aggregated form is more bioactive, in one recent study it was reported that lipid A (the lipid part of lipopolysaccharide, LPS, from *E. coli*) forms small aggregates, and these show bioactivity (tumor necrosis factor TNFα production cell assays), whereas monomer does not.[46] Earlier reports provided conflicting results. Whereas Shnyra et al. reported that aggregated LPS shows enhanced endotoxic activity compared to less aggregated form,[47] Takayama et al. found enhanced stimulating activity of LPS in a disaggregated monomeric state.[48,49] Although this work is on nonpeptide systems, related lipopeptides are also involved in immune response and it will be interesting to examine whether there is any difference in bioactivity of aggregated vs monomeric forms of such peptide conjugates.

Our group recently showed that the aggregation state of Toll-like (TLR) receptor agonist lipopeptides depends on the number of palmitoyl lipid chains attached to the hexapeptide sequence CSK_4,[50] although this has not yet been correlated to bioactivity. The lipopeptides with one or two lipid chains self-assembled into spherical micelles with a disordered peptide conformation, whereas the variant with three lipid chains forms a population of flexible nanotape structures based on β-sheet bilayers. In another study, it was shown that the association number of micelles formed by liraglutide, a lipidated glucagon-like peptide 1 (GLP-1) agonist, is pH-dependent, although this was not correlated to bioactivity.[51]

6. PA/BIOPOLYMER COMPOSITES

The potential to combine the properties of PAs and peptides with those of biopolymers (e.g., structural and mechanical properties, ready availability) has begun to be investigated, leading to the creation of novel hybrid biomaterials with remarkable and unique structural and functional properties. Hybrid systems examined in early studies include PAs with polysaccharides,[52−55] PAs with recombinant structural proteins,[56] or amyloid peptides.[57] Also recently studied are hybrid materials from PAs with polysaccharides such as sodium alginate including graphene oxide in the system to provide novel and/or enhanced properties (structural, mechanical, electronic).[58−61] Stupp and co-workers reported the first observation of membrane sac formation at the interface of aqueous solutions of high-molecular-weight polysaccharide (hyaluronic acid) and a cationic designer PA.[52] The membrane formation was proposed to result from the formation of a PA fibril network diffusion barrier, leading to polysaccharide nanofibril bundle growth perpendicular to the interface.[52] The sacs enclosing PA gel were

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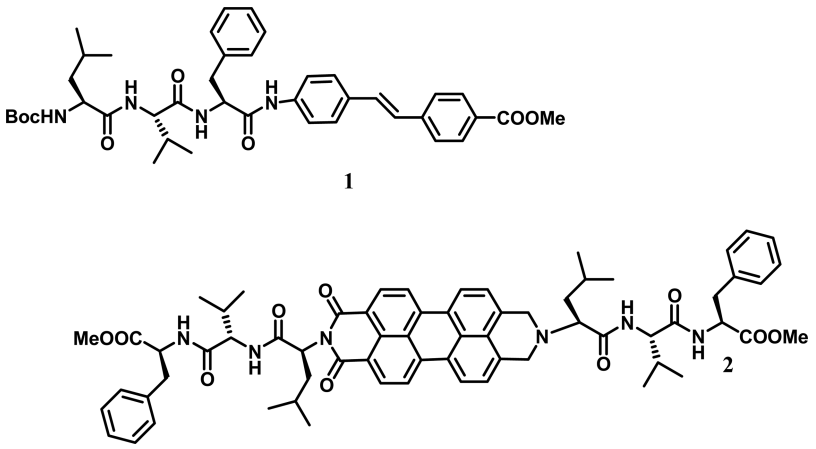

Figure 4. Structure of compounds **1** and **2** studied by Banerjee's group,[67] an equimolar mix of which in *o*-dichlorobenzene emits white light. Reproduced in part from ref 67 with permission of the Royal Society of Chemistry.

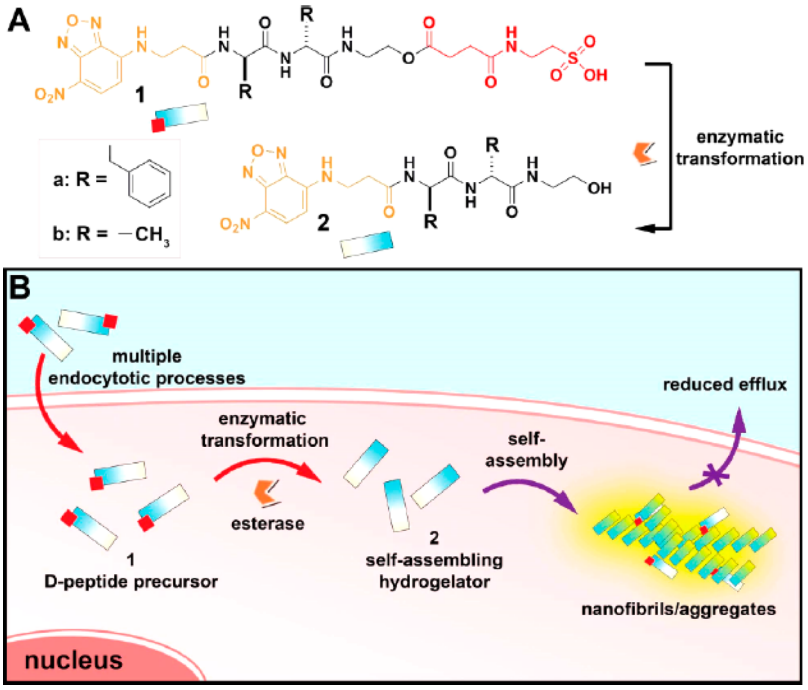

Figure 5. Intracellular esterase transforms a D-peptide−taurine conjugate (with N-terminal fluorophore) into an aggregating molecule, which forms fibrils accumulating inside cells.[71] Reprinted with permission from ref 71, Copyright 2015 American Chemical Society.

found to support stem cell growth and slow release of encapsulated proteins. In subsequent work, the mechanical properties and membrane permeability were examined in more detail.[53] Membranes formed by PAs bearing the KLAKLAK sequence (with anticancer activity) mixed with hyaluronic acid were also fabricated and their cytotoxicity toward breast cancer cells was examined.[54] A change in PA aggregate structure from cylindrical fibrils to spheres was also noted for this system.[54] Membranes formed by complexation of a PA bearing a heparin-binding sequence with several polysaccharides (including heparin) have been prepared and their structure probed by SAXS and electron microscopy.[55] Interestingly, in some cases, evidence for cubic phase structure within the membrane instead of lamellar or hexagonal ordering was observed.[55] Recently, Mata and co-workers have demonstrated that complexation of cationic PAs with elastin-like peptides produces robust membranes with remarkable mechanical properties including the ability to draw out membrane tubes, and to extend tubules from the tube walls.[56] These materials could be used to create substrates able to support stem cell growth, showing their great potential in tissue engineering applications.[56] Our group has recently prepared hybrids of a cationic PA with sodium alginate, and soft or hard capsules could be fabricated depending on the incorporation of graphene oxide.[62] Addition of sodium alginate leads to a transition from micelles, which the PA molecules form on their own, into bilayer structures which comprise the structural motif of macroscopic membrane structures. A novel mechanism of membrane formation is proposed. These materials also have interesting antimicrobial properties.[62]

7. FUNCTIONAL π-STACKING PEPTIDE CONJUGATES

There has been a considerable amount of research on peptide conjugates with bulky N-terminal substituents, which among other interesting properties are able to form hydro- and organo-

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gels. The aggregation properties of these molecules are enhanced by π-stacking interactions of the N-terminal substituents such as Fmoc [Fluorenylmethyloxycarbonyl] or naphthalene. Since this subject has been recently reviewed by several groups,[2,63−65] all this prior work is not discussed again here. In one recent impressive example, Banerjee's group has developed gelators based on a naphthalene diimide core with symmetrically attached alkylated peptides, and showed that the fluorescence properties change upon formation of J-aggregate structures.[66] In another development, they discovered a two-component peptide-based system exhibiting white light emission.[67] This was observed for mixtures of **1** and **2** (Figure 4) where **1** contains a stilbene electron-donating moiety, and **2** contains a perylene diimide electron acceptor. An equimolar mixture of **1** and **2** in *o*-dichlorobenzene produces white light.[67]

It has recently been shown that conjugation of the fluorophore FITC [fluorescein isothiocyanate] to the simple dipeptide dileucine produces a cyto-compatible conjugate that is taken up by dermal or corneal fibroblasts in contrast to FITC itself.[68] Co-localization imaging experiments show that FITC-LL segregates in peri-nuclear and intracellular vesicle regions.

8. USE OF ENZYMES TO TUNE SELF-ASSEMBLY

Enzymes are natural catalysts, and being proteins, their binding sites are peptide sequences and their substrates can also be proteins or peptides. Recently, attention has been focused on the use of enzymes to tune the self-assembly of peptide-based materials. Xu's group pioneered the use of enzymes to modulate the hydrophobicity of peptide conjugates such that they self-assemble into fibrils (which can in turn entangle to form hydrogels). A variety of enzymes including phosphatases/kinases or thermolysin or esterases among others can be used for this purpose. Ulijn's group and others have made extensive use of this concept, using for example esterases such as subtilisin to link Fmoc-peptide methyl esters (and other similar conjugates with bulky hydrophobic N-terminal units) and peptides into fibril-forming gelators. Thermolysin has also been used by this group to link short Fmoc-peptides with uncapped C termini to methyl esters of amino acids. This work has been reviewed elsewhere.[69,70]

The Xu group has recently shown that intracellular esterase can be used to drive the aggregation of a conjugate of taurine (2-aminoethanesulfonic acid), with a peptide such as a short D-amino acid peptide (resistant to proteolysis) via breakage of the ester linkage between taurine and peptide in vivo. Aggregation enhances cellular uptake (in fact it reduces cellular efflux of the aggregated form, Figure 5).[71] This is only one example of a great deal of interesting recent work from this group, but unfortunately lack of space prohibits further discussion herein. Exploiting a similar concept, a lipopeptide susceptible to degradation by the cancer-related enzyme matrix metalloprotease 7 (MMP-7) aggregates to form a fibrillar hydrogel upon endogenous MMP-7 cleavage within cancer cells.[72] This leads to significant cancer cell death.

In a subtle demonstration of the power of enzymatic biotransformations, Gianneschi's group showed that enzymatic farnesyl transfer to peptides leads to PAs that self-assemble into fibrils.[73] The farnesyl group was transferred from a farnesyl-coA conjugate using a phosphopantetheinyl transferase (Figure 6).

The serine protease α-chmyotrotrypsin can be used to cleave a Phe-containing lipopeptide C_{16}−KKFFVLK at the aromatic residues.[74] The parent PA self-assembles into helically twisted ribbons (and nanotubes),[75] but the cleaved PAs C_{16}−KKF and

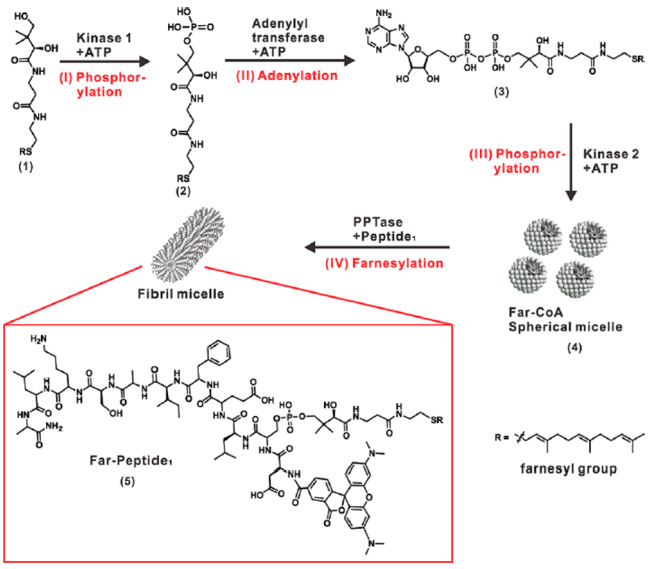

Figure 6. Process for farnesylation of peptide and self-assembled motif of Far-peptide **5** compared to micelles of Far-CoA (**4**).[73] The starting material is a farnesyl−pantetheine conjugate (**1**) which is phosphorylated by Kinase 1 to generate **2** which in turn is adenylated using an adenyl transferase to generate the dephospho-Far-CoA 3. Following phosphorylation of **3** with Kinase 2, **4** was formed which spontaneously self-assembles into spherical micelles. Transfer of the farnesyl group onto Peptide 1 (an 11-amino-acid fragment of the natural protein substrate for PPTase enzymes) was achieved via recognition of the pantetheine adaptor molecule, leading to **5** which self-assembles into fibrils. Reprinted with permission from ref 73, Copyright 2015 American Chemical Society.

C_{16}−KKFF form small spherical micelles.[74] The enzyme elastase can be used to break up hydrogels formed by the self-assembly of the model surfactant-like alanine-rich peptide KA_6E, which forms hydrogels containing tape-like fibrils.[76]

9. HIGH THROUGHPUT METHODS

High throughput methods offer a means to efficiently and rationally assess properties of a peptide or peptide amphiphile, such as bioactivity (e.g., cytocompatibility) or physical properties. In a pioneering work, Ulijn's group have screened all 8000 (20^3) tripeptides (based on combinations of natural amino acids) for their ability to form hydrogels.[77] This led to the identification of several novel tripeptides able to form hydrogels at neutral pH. High throughput methods, which are already extensively used to synthesize and screen peptide-based materials, are likely to be powerful tools in the future in assessing the aggregation properties and bioactivities of various classes of peptide conjugates.

10. SEQUENCED PEPTIDES

The term sequenced peptides here refers to alternating or bola-amphiphilic peptides, although one class of such molecules comprises both features, i.e., an alternating peptide central sequence flanked by terminal charged residues, termed multi-domain peptides (MDPs) by the Hartgerink group.[78] The aggregation properties of sequenced peptides and bola-amphiphilic peptides has recently been investigated by several groups and a review on this topic was published in 2015.[79] However, there have been subsequent interesting papers briefly highlighted here. The alternating peptide RFRFRFRF self-assembles into very well ordered β-sheet fibrils.[80] The peptide

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produces a highly aligned and feature-filled fiber X-ray diffraction pattern which permits a structural model to be proposed, and alignment of solutions under flow was also observed by SAXS.[80] In the category of bola-amphiphiles, the peptide RFL_4FR forms nanosheets and films of this peptide can support the growth of fibroblasts.[81] The anionic analogue EFL_4FE forms nanotubes instead which slowly develop in aqueous solution over a period of days.[82]

11. CONCLUSIONS

This Topical Review has focused on several interesting recent developments in the field of self-assembling peptide conjugates. In the space available, a comprehensive review was not possible and we have highlighted instead a few examples of recent papers (mainly from the last 3−4 years) that attracted our attention as they report novel and/or significant developments, likely to impact on research in this field. There are many other fascinating challenges in exploiting this remarkable class of self-assembling molecule for future applications in biomedicine and bioengineering among others. We keenly anticipate new discoveries as this field moves forward.

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Notes

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